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Docket No. 11823-9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of )  
Cary L. Queen et al. )  
Serial No.: 07/310,252 )  
Filed: February 13, 1989 )  
For: DESIGNING IMPROVED )  
HUMANIZED IMMUNOGLOBULINS )  
)

INFORMATION DISCLOSURE  
STATEMENT UNDER  
37 CFR 1.97 AND 1.98

Hon. Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

Sir:

The following references cited on attached form PTO-1449  
are being called to the attention of the Examiner. A copy of each  
is enclosed. It is requested that the Examiner make them of  
record.

No.	Patent #	Patent Date	Patentee
AA	4,816,397	3/28/89	Boss et al.
AB	4,816,567	3/28/89	Cabilly et al.

No.	Publication No.	Publication Date	Country
AC	0,239,400	9/30/87	EPO
AD	0,173,494	3/5/86	EPO
AE	0,184,187	6/11/86	EPO
AF	WO89/01783	3/9/89	PCT
AG	WO86/5513	9/25/86	PCT
AH	WO87/02671	5/7/87	PCT
AI	0,171,496	2/19/86	EPO
AJ	0,266,663	6/11/88	EPO
AK	2,188,941	10/14/87	GB

No. Author, Name of Publication, Pages, Dates

A1 Vitteta et al., Science 238:1098-1104 (1987).  
A2 Ellison et al., Nucleic Acids Res. 10:4071- (1982).

A3 Hieter et al., Cell 22:197-207 (1980).

A4 Sharon et al., Nature 309:364-367 (1984).

A5 Takeda et al., Nature 314:452-454 (1985).

A6 Tan et al., J. Immunol. 135:3564-3567 (1985).

A7 Morrison et al., Proc. Natl. Acad. Sci. 81:6851-6859 (1984).

A8 Boulianne et al., Nature 312:643-646 (1984).

A9 Neuberger et al., Nature 314:268-270 (1985).

A10 Morrison, S.L., Science 229:1202-1207 (1985).

A11 Sahagan et al., J. Immunol. 137:1066-1074 (1986).

A12 Liu et al., Gene 54:33-40 (1987).

A13 Better et al., Science 240:1041-1043 (1988).

A14 Waldmann, T.A., Science 232:727-732 (1986).

A15 Leonard et al., J. Biol. Chem. 260:1872-1880 (1985).

A16 Uchiyama et al., J. Immunol. 126:1393-1397 (1981).

A17 Farrar, J., Immunol. Rev. 63:129- 166 (1982).

A18 Greene et al., in Progress in Hematology XIV, E. Brown, ed., Grune and Statton, New York (1986) p.283-301.

A19 Verhoyen et al., Science 239:1534-1536 (1988).

A20 Jones et al., Nature 321:522-525 (1986).

A21 Hale et al., Lancet December 17, 1988, pp. 1394-1399.

A22 Chothia, C. and A.M. Lesk, J. Mol. Biol. 196:901-917 (1987).

A23 Reichmann et al., Nature 332:323-327 (1988).

A24 Bird et al., Science 242:423-426 (1988).

A25 Huston et al., Proc. Natl. Acad. Sci. U.S.A. 85:5879-5883 (1988).in Progress in Hematology XIV, E. Brown, ed., Grune and Statton, New York (1986) p.283.

The above documents are considered pertinent for the following reasons:

References A14, A15, A16, A17 and A18 describe IL-2 and IL-2 receptors and antibodies thereto, including anti-Tac antibody, the humanization of which is an example in the present application.

References A2, A3, A12 and A22 describe structural aspects of immunoglobulins.

References AA, AB, AD, AE, AG, AH, AI, AJ, A4, A5, A6,

A7, A8, A9, A10, A11, A13, A19, A24 and A25 generally describe recombinant immunoglobulins, particularly chimeric immunoglobulins.

Reference AK describes monoclonal antibodies to IL-2 receptors and also mentions chimeric antibodies, e.g., at page 2, lines 21-27.

References AC, AF, A20, A21 and A23 describe production and use of humanized immunoglobulins (i.e., containing non-native complementarity determining regions).

Reference A1 describes immunotoxins.

Respectfully submitted,  
TOWNSEND and TOWNSEND

By W.M. Smith  
William M. Smith  
Reg. No. 30,223

Date: 5-26-90

Steuart Street Tower  
One Market Plaza  
San Francisco, California 94105  
Telephone: (415) 326-2400

EXAMINER	W. Ladd
DATE CONSIDERED	1/25/91

A2	Author, Title, Date, Pertrinente Pages, Etc.	Vitteta et al., "Redesigning Nature's Positions to Create Anti-Tumor Reagents," Science 238:1098-1104 (1987).	Zimmer et al., "The nucleotide sequence of a human immunoglobulin C(gamma)1 gene," Nucleic Acids Res. 10:4071-4072 (1982).
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#### OTHER REFERENCES

Exam Number	Document No.	Date	Count	Subject Class	Yes	No
AC	0,239,400	9/30/87	EPO			
AD	0,173,494	3/5/86	EPO			
AE	0,184,187	6/11/86	EPO			
AF	W089/01783	3/9/89	PC-T			
AG	W086/05513	9/25/86	PC-T			
AH	W087/02671	5/7/87	PC-T			
AI	0,171,496	2/19/86	EPO			
AT	0,266,663	6/11/88	EPO			
AK	2,188,941	10/14/87	GB			

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Exam/Inter No.	Document No.	Date	Name	Class	Subject Class	File Approb.
AA	4,816,397	3/28/89	Boss et al.	—	—	—
AB	4,816,567	3/28/89	Capilly et al.	—	—	—

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LIST OF REFERENCES		APPLICANT(S): CARRY L. QUEEN ET AL. Group No: 185	Filing Date: February 13, 1989 Page No: 1 of 4
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A10 Morrisson, S.L., "Transfectoromas Provide Novel Chimeric Antibodies," *Science* 229:1202-1207 (1985).

A9 Neuberger et al., "A human-specific chimeric IgE antibody with human physiologic effector function," *Nature* 314:268-270 (1985).

A8 Boulianne et al., "Production of functional chimeric mouse/human antibody," *Nature* 312:643-646 (1984).

A7 Morrisson et al., "Chimeric human antibody molecules: Mouse antigen-binding domains with human constant region domains," *Proc. Natl. Acad. Sci.* 81:6851-6859 (1984).

A6 Tzan et al., "A Human-Mouse chimeric IgM antibody with constant region sequences," *Nature* 314:452-454 (1985).

A5 Takeeda et al., "Construction of a chimeric protein consisting of human immunoglobulin genes containing mouse variable and human immunoglobulin sequences," *Nature* 309:364-367 (1984).

A4 Sharon et al., "Expression of a V<sub>H</sub>C<sub>L</sub> chimeric protein in mouse myeloma cells," *Nature* 309:364-367 (1984).

A3 Hietter et al., "Cloned Human and Mouse kappa immunoglobulin segments," *Cell* 22:197-207 (1980).

A2 Author, Title, Date, Pertinent Pages, Etc.

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A18 Greene et al., "Growth of Human T Lymphocytes: An Analysis of Hematology XVI" 2 and Its Cellular Receptor", in *Progress in Interleukin-2 in the Induction of Cytotoxic T Cell and Antibody-forming B Cell Receptors*, Immuno. Rev. 63:129-166 (1982).

A17 Fartrar, J., "The Biochemistry, Biology, and Role of Interleukin-2 in the Induction of Cytotoxic T Cell and Antibody-forming B Cell Receptors", Immuno. Rev. 63:129-166 (1982).

A16 Uchiyama et al., "A Monoclonal Antibody (anti-Tac) Reactive with Activated and Functionally Mature Human T-cells", J. Immunol. 136:1393-1397 (1981).

A15 Leonardi et al., "The Human Receptor for T-cell Growth Factor", J. Biol. Chem. 260:1872-1880 (1985).

A14 Waldmann, T.A., "The Structure, Function, and Expression of Interleukin-2 Receptors on Normal and Malignant Lymphocytes", Science 232:727-732 (1986).

A13 Better et al., "Escerichia coli Secretion of an Active Chimeric Antibody Fragment", Science 240:1041-1043 (1988).

A12 Liu et al., "Expression of mouse: human immunoglobulin heavy-chain cDNA in Lymphoid Cells", Gene 54:33-40 (1987).

A11 Shagahan et al., "A Genetically Engineered Murine/Human Chimeric Antibody Receptor Specificity for Human Tumor-Associated Antigen", J. Immunol. 137:1066-1074 (1986).

A10 Author, Title, Date, Pertinent Pages, Etc.

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A19	Verhoyen et al.	"Reshaping Human Antibodies: Grafting an Antilysozyme Activity", Science 239:1534-1536 (1988).	322:522-525 (1986).
A20	Jones et al.	"Replacing the Complementarity-determining Regions in a Human Antibody with those from a mouse", Nature 322:522-525 (1986).	326:901-917 (1987).
A21	Hale et al.	"Reshaped Human Monoclonal Antibody CAMPATH-1H", Lancelet December 17, 1988, pp. 1394-1399.	Reshaped Human Monoclonal Antibody CAMPATH-1H", Lancelet December 17, 1988, pp. 1394-1399.
A22	Chothia, C. and A.M. Lesk	"Canonical Structures for the Hypervariable Regions of Immunoglobulins", J. Mol. Biol.	Reichmann et al., "Reshaping human antibodies for therapy", Nature 332:323-327 (1988).
A23			Geilicence 242:423-426 (1988).
A24	Bird et al.	"Single-chain Antibody Binding Proteins", Geilicence 242:423-426 (1988).	
A25	Huston et al.	"Protein engineering of antibody binding sites: Recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli", Proc. Natl. Acad. Sci. U.S.A. 85:5879-5883 (1988).	Single-chain Fv antibody produced in Escherichia coli, Proc. Natl. Acad. Sci. U.S.A. 85:5879-5883 (1988).

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